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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,657	WADA ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *,3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41-44, 51, 53, 55-58, 60-75, 78-79, 84, 86, 88-89, 91-93, 95-96, 98-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,3,4,8-14,16-27,29,31,32,35,37-39,41-44,51,53,55-58,60-75,78,79,84,86,88,89,91-93,95,96 and 98-100.

DETAILED ACTION

1. This action is in response to papers filed 12/19/2008.

2. Currently Claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41-44, 51, 53, 55-58, 60-75, 78-79, 84, 86, 88-89, 91-93, 95-96, 98-100 are pending. Claims 2, 5-7, 15, 28, 30, 33-34, 36, 40, 45-50, 52, 54, 59, 76-77, 80-83, 85, 87, 90, 94, 97 have been cancelled.

3. The following rejections are newly applied. Where applicable response to arguments follows.

4. This action is NONFINAL.

Withdrawn Rejections/Objections

5. The rejections of the claims under 35 USC 102(b) and 35 USC 103(a) over Kawabata et al. made in sections 8-14 made in the previous office action are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 39-41 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 39 and 41 are indefinite. Claim 39 is drawn to contacting "(a) the sample containing the analyte, (b) either the analyte labeled by a detectable marker…thereby

forming a first complex of the analyte in the sample and one or more conjugates and a second complex of either the labeled analyte." It is not clear if the analyte of part b is the same analyte of the sample containing the analyte or some other undefined analyte and therefore there is insufficient antecedent basis for “the analyte” of b.

The last step of the claim is determining an amount of the analyte in the sample on the basis of the measured amount. In step iv, the measured amounts are the separated second complex which has the labeled analyte and the affinity/charged complex; and the amount of the free labeled analyte or the free labeled analogue. Step i, is drawn to two analytes, an analyte in the sample and a labeled analyte. Step iv measures only the labeled analyte. Therefore it is unclear how the determination of the analyte in the sample is determined from these measurements.

Claim 42 is drawn to contacting "(a) the sample containing the analyte, (b) either the analyte bound to a charged" It is not clear if the analyte of part b is the same analyte of the sample containing the analyte or some other undefined analyte and therefore these is insufficient antecedent basis for “the analyte” of b.

Claim 44 is indefinite because the claim recites the abbreviations AFP, hCG, TSH, FSH, LH, CA19-9, CA125, PSA, HBsAg, and T4, which should be spelled out in all independent claims in the interest of clarity. For example, a search of Genecard for the abbreviation of “FSH” provided hits for follicle stimulating hormone, beta polypeptide and the follicle stimulating hormone receptor. As such it is not clear in the arts that this abbreviation is a follicle stimulating hormone receptor or a follicle stimulating hormone, beta polypeptide. The mere recitation of an acronym is insufficient to indicate the metes

and bounds of the claim. The use of the abbreviations causes the claims to be indefinite, because abbreviations often have multiple meanings in the art and the meaning can change over time. Amendment of the claims to include the full name represented by the abbreviation would remove this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 51, 60-65, 68-70, 72-75, 78-79, 84, 86, 88-89, 91-92, and 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (WO 02/082083 A1 published 10/17/2002) in view of Janssen et al. (US Patent 5611903 March 18, 1997).

Citations are from the National Stage (US Patent Application 2004/0144649 July 29, 2004). The national stage is deemed an English language translation of the PCT.

With regard to Claim 1, Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with a nucleic acid chain binding affinity substance marker (e.g. an affinity molecule conjugated with a charged particle) (p. 2 paragraph 0013). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (abstract and p. 2 paragraph 13-14). The nucleic acid chain would be considered the charged molecule since nucleic acid has a negative charge.

The instant specification does not define the term microfluidic device. Therefore the term is broadly interpreted as any microscopic component designed to handle liquid flow. Kawabata et al. teaches a method for separation by electrophoresis (p. 2 paragraph 15). Kawabata et al. however does not teach a polyanion. Kawabata et al. teaches separating the complex using capillary electrophoresis (e.g. a microfluidic device) with a channel diameter preferably 1 to 200 microns (p. 10 paragraph 93). The capillary electrophoresis in Kawabata et al is interpreted to be a microfluidic device.

Kawabata et al. teaches a method for measuring (detecting) a target (analyte) (abstract).

With regard to Claim 9, Kawabata et al. teaches a nucleic acid chain affinity substance is labeled with a marker (Figure 2).

With regard to Claims 11, 12, and 13, Kawabata et al. teaches the binding of "protein" and "peptide chain"; "antigen" and "antibody"; "sugar chain" and "lectin"; "enzyme" and "inhibitor"; and "receptor" and "ligand" (p. 5 paragraph 55).

With regard to Claims 14, 16-17, Kawabata et al. teaches the charged carrier molecule (referred to as nucleic acid chain binding affinity substance) is a nucleic acid chain (anionic) (p. 4 paragraph 50).

With regard to Claims 18, Kawabata et al. teaches the charged carrier is a nucleic acid chain (nucleotide chain, DNA) (p. 4 paragraph 50). Kawabata et al. teaches the nucleic acid chain used may be prepared by chemical synthesis (synthetic) (p. 4 paragraph 52).

With regard to Claims 19-21, Kawabata et al. teaches a method of labeling the nucleic acid with a linker, such as, Sulfo-SMPB (sulfosuccinimidyl) (succinimide group) and a marker (p. 7 paragraph 64, 66, and 67).

With regard to Claims 22, Kawabata et al teaches a nucleic acid chain attached to an affinity substance and labeled with a marker (Figure 2). The conjugate is the nucleic acid chain attached to the affinity substance. Kawabata et al. teaches the nucleic acid chain is labeled (p. 7 paragraph 64, 66, and 67) therefore when complexed to the charged molecule the affinity molecule is labeled.

With regard to Claim 27, Kawabata et al. teaches the use of fluorescent dyes and radioactive tracers (p. 6 paragraph 62).

With regard to Claim 29, Kawabata et al. teaches the separation media can be comprised of polyethylene glycol, polyacrylamide, polyethylene oxide, or polyvinylpyrrolidone (p. 9 paragraph 85).

With regard to Claim 35, Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 10 paragraph 93).

With regard to Claim 37, Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with a nucleic acid chain binding affinity substance marker (e.g. an affinity molecule conjugated with a charged particle) (p. 2 paragraph 0013). The conjugate has a detectable marker (p. 2 paragraph 13). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (abstract and p. 2 paragraph 13-14). The nucleic acid chain would be considered the charged molecule and nucleic acid have a negative charge.

Kawabata et al. teaches a method for separation by electrophoresis (p. 2 paragraph 15). Kawabata et al. however does not teach a polyanion. Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 10 paragraph 93). Kawabata et al. teaches a method for measuring (detecting) a target (abstract).

With regard to Claim 43, Kawabata et al. teaches targets comprising serum, plasma, urine, feces, and environmental samples (p. 9 paragraph 85).

With regard to Claim 44, Kawabata et al. teaches a target comprising AFP, FSH, TSH, LH, HIV, CA10-19, CA125, PSA, or T4 (p. 5 paragraph 56).

With regard to Claim 51, this claim requires all the limitations of Claim 1 plus each charged carrier molecule has a net negative charge. As discussed with regard to Claim 1, the charged carrier molecule of Kawabata et al. has a net negative charge because the charged carrier molecule is a nucleic acid. Further the claims require a concentration channel filled with a concentration media and a polyanion. The instant specification does not define concentration media. Therefore the separation media would be considered a concentration media because a solution is poured into the capillary and only analytes are separated out thereby concentrating the analyte.

With regard to Claims 60-62, Kawabata et al. teaches the charged carrier is a nucleic acid chain (nucleotide chain, DNA) (p. 4 paragraph 50). Kawabata et al. teaches the nucleic acid chain used may be prepared by chemical synthesis (synthetic) (p. 4 paragraph 52).

With regard to Claims 63-65, Kawabata et al. teaches a method of labeling the nucleic acid with a linker, such as, Sulfo-SMPB (sulfosuccinimidyl) (succinimide group) and a marker (p. 7 paragraph 64, 66, and 67).

With regard to claims 68-69, Kawabata et al. teaches the binding of "protein" and "peptide chain"; "antigen" and "antibody"; "sugar chain" and "lectin"; "enzyme" and "inhibitor"; and "receptor" and "ligand" (p. 5 paragraph 55).

With regard to Claim 70, Kawabata et al. teaches an affinity molecule which is a Fab or antibody (paragraph 31 p. 3).

With regard to Claim 72-73, Kawabata et al. teaches a nucleic acid chain affinity substance is labeled with a marker (Figure 2).

With regard to Claims 74, Kawabata et al teaches a nucleic acid chain attached to an affinity substance and labeled with a marker (Figure 2). The conjugate is the nucleic acid chain attached to the affinity substance. Kawabata et al. teaches the nucleic acid chain is labeled (p. 7 paragraph 64, 66, and 67) therefore the affinity molecule is labeled.

With regard to Claim 75, Kawabata et al. teaches the use of fluorescent dyes and radioactive tracers (p. 6 paragraph 62).

With regard to Claim 86, Kawabata et al. teaches the separation media can be comprised of polyethylene glycol, polyacrylamide, polyethylene oxide, or polyvinylpyrrolidone (p. 9 paragraph 85).

With regard to Claim 92, Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 10 paragraph 93).

With regard to Claim 95, Kawabata et al. teach at least two conjugates (e.g. affinity and nucleic acid marker) which bind to the target (analyte) at different sites (Figure 4).

However, with regard to steps ii-iv, Kawabata et al. does not teach that the separation channel is further filled with a polyanion.

With regard to Claims 1 and 51, Janssen et al. teaches adding a polyanion to a capillary buffer in a capillary electrophoresis detection method (abstract). Janssen et al. teaches that the polyanion can be a polysaccharide derivative, a synthetic polymer derivative, a polyacidic amino acid, a polynucleotide, a polyphosphate, a polyphosphonate, a polyphosphoric acid, or heparin (column 9 lines 15-20 and table 2). Janssen et al teaches the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated (column 8 lines 1-6).

With regard to claims 3-4, Janssen et al. teaches that the polyanion can be a polysaccharide derivative, a synthetic polymer derivative, a polyacidic amino acid, a polynucleotide, a polyphosphate, a polyphosphonate, a polyphosphoric acid, or heparin (column 9 lines 15-20 and table 2).

With regard to claim 8, Janssen et al. teaches that the polyanion comprises heparin sulfate (table 2).

With regard to Claims 31 and 32, Janssen et al. teaches a method wherein the polyanion comprises about 1% by volume of the media in the capillary (column 10 lines 4-5).

With regard to claims 78-79, Janssen et al. teaches that the polyanion can be a polysaccharide derivative, a synthetic polymer derivative, a polyacidic amino acid, a polynucleotide, a polyphosphate, a polyphosphonate, a polyphosphoric acid, or heparin (column 9 lines 15-20 and table 2).

With regard to claim 84, Janssen et al. teaches that the polyanion comprises heparin sulfate (table 2).

With regard to Claims 88-89, Janssen et al. teaches a method wherein the polyanion comprises about 1% by volume of the media in the capillary (column 10 lines 4-5).

With regard to claim 91, Janssen et al. teaches that polyanions comprise about 1% by volume and that one of the polyanions can be heparin sulfate (Column 10 lines 4-5 and Table 2).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify method of detecting or identifying an analyte of interest in a sample of Kawabata et al. to include in the step of providing a microfluidic device a separation channel which has a polyanion in a separation buffer as taught by Janssen et al. The ordinary artisan would have been motivated to modify the method of detecting or identifying an analyte of interest in a sample of Kawabata et al. to include in the step of providing a microfluidic device a separation channel which has a

polyanion in a separation buffer as taught by Janssen et al., because Janssen et al teaches the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated (column 8 lines 1-6) therefore the use of polyanions allows for better elution of the analyte from complexes.

Response to Arguments

The reply traverses the rejection. A summary of the arguments set forth in the reply is provided below with response to arguments following.

(A) The reply traverses the rejection of the claims under 35 USC 102(b) with regard to the EP publication date (p. 23 1st paragraph).

This argument has been thoroughly reviewed and has been found persuasive.

It is acknowledged that the EP publication was published after the priority date of the instantly pending application. However, the WO document (WO 02/082083 A1) published 10/17/2002 is being used in the above 35 USC 103(a). The date of the WO document is considered a 102(a) date.

(B) The reply asserts that the claims require contacting the sample with an affinity molecule/charged carrier conjugate, electrophoretically separating or concentrating the materials wherein the separation/concentration channel includes a polyanion (p. 24 bullets). The reply asserts that Kawabata et al. does not teach using a polyanion specifically added to the separation media (p. 24 1st full paragraph).

The reply asserts that Kawabata et al. does not teach the limitations of Claim 39, 42, and 93 (p. 25-26)

The reply asserts that with regard to Claim 51, Kawabata et al. does not teach the use of a polyanion (p. 26 2nd full paragraph).

These arguments have been thoroughly reviewed and have been found partially persuasive.

Kawabata et al does not teach the limitations of 39, 42, and 93 and as such these claims are not rejected in the above 35 USC 103(a) rejection.

Though, Kawabata et al. does not teach using polyanions. However, the combination of Kawabata et al. and Janssen et al. teaches using polyanions because Janssen et al. teaches adding a polyanion to a capillary buffer in a capillary electrophoresis detection method (abstract). Janssen et al. teaches that the polyanion can be a polysaccharide derivative, a synthetic polymer derivative, a polyacidic amino acid, a polynucleotide, a polyphosphate, a polyphosphonate, a polyphosphoric acid, or heparin (column 9 lines 15-20 and table 2). Janssen et al teaches the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated (column 8 lines 1-6).

9. Claims 53, 55-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (WO 02/082083 A1 published 10/17/2002) in view of Janssen et al. (US Patent 5611903 March 18, 1997) as applied to Claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 51, 60-65, 68-70, 72-75, 78-79, 84, 86, 88-89, 91-92, and 95 and further in view of Kaniansky et al. (Analytical chemistry 2000 Vol. 72 p. 3596).

Citations are from the National Stage (US Patent Application 2004/0144649 July

29, 2004). The national stage is deemed an English language translation of the PCT.

Kawabata et al. and Janssen et al. teach a method detecting or identifying an analyte of interest in a sample by electrophoretically separating an analyte coupled to an affinity/charged conjugate in a separation buffer comprising a polyanion. However, Kawabata et al. and Janssen et al. do not teach a step of connecting the microchannel (e.g. the capillary column) to a concentration channel.

With regard to Claims 53, Kaniansky et al. teaches a method of using a capillary electrophoresis chip with a two separation channel coupling (Abstract). Kaniansky et al. teaches using ITP (e.g. Concentration channel) as a concentration pretreatment of the analyte (Abstract). Therefore Kaniansky et al. teaches a microchannel fluidically connected to a concentration channel. The claim requires at least one microscale dimension of between about 0.1 and 500 microns. The limitation does not require that the concentration channel be that size but rather the microfludiic device should have a microscale dimension of between about 0.1 and 500 microns. Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 10 paragraph 93).

With regard to Claim 55-56, ITP is based on the mobility differences of the solution placed into the column, therefore, dependent on the size and charge of the components in the solution including the charged carrier, the components either get concentrated in a solution or trapped in the membrane. Therefore ITP utilized the charge of the complex (e.g. the charged carrier, the analyte, and the antigen) to move through the membrane whereas other components in the sample do not.

With regard to Claims 57-58, Kaniansky et al. teaches using isotachophoresis (ITP).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify method of detecting or identifying an analyte of interest in a sample of Kawabata et al. and Janssen et al. to include in the step of providing a microfluidic device a step of providing a concentration channel such as the ITP concentration method as taught by Kaniansky et al. The ordinary artisan would have been motivated to modify method of detecting or identifying an analyte of interest in a sample of Kawabata et al. and Janssen et al. to include in the step of providing a microfluidic device a step of providing a concentration channel such as the ITP concentration method as taught by Kaniansky et al. because Kaniansky et al. teaches using an ITP concentration pretreatment quantified test analytes by 1-2% RSD (Abstract). Kaniansky et al. teaches a well-defined ITP concentration of the analyte can be integrated into the separation method of a capillary channel chip (Abstract). By using the ITP concentration channel the ordinary artisan can increase the concentration of the analyte in the solution and thereby increase the detection and concentration of the analyte by the method of Kawabata et al. and Janssen et al.

10. Claim 66 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (WO 02/082083 A1 published 10/17/2002) in view of Janssen et al. (US Patent 5611903 March 18, 1997) as applied to Claims 1, 3-4, 8-9, 11-14, 16-22, 27, 29, 31-32, 35, 37, 43-44, 51, 60-65, 68-70, 72-75, 78-79, 84, 86, 88-89, 91-92, and 95 and further in view of Brown et al. (The journal of biological chemistry 1994 vol 269 p.

26801).

Citations are from the National Stage (US Patent Application 2004/0144649 July 29, 2004). The national stage is deemed an English language translation of the PCT.

Kawabata et al. and Janssen et al. teach a method detecting or identifying an analyte of interest in a sample by electrophoretically separating an analyte coupled to an affinity/charged conjugate in a separation buffer comprising a polyanion. The combination of Kawabata et al. and Janssen et al. teaches a step of an affinity molecule/charged carrier molecule in which the charged carrier molecule comprises an oligonucleotide attached to a label. Kawabata et al. and Janssen et al. do not teach that the synthetic sequence (e.g. oligonucleotide) comprises phosphorothioate.

With regard to Claim 66, Brown et al. teaches a method of mobility shift assays which uses phosphorothiate-modified oligonucleotides (abstract). Brown et al. teaches that phosphorothioate modified oligonucleotides exhibit greater protein binding than unmodified oligonucleotides (abstract).

Therefore it would be prima facie obvious to modify the method of Kawabata et al. and Janssen et al. to further include a modification of the oligonucleotide which is attached to the label in the charged carrier molecule of Kawabata et al. to include phosphorathiate modification of Brown et al. The ordinary artisan would be motivated to modify the oligonucleotide used in the method of Kawabata et al. and Janssen et al. to include phosphorothiate because Brown et al. teaches phosphorothioate modified oligonucleotides exhibit greater protein binding than unmodified oligonucleotides (abstract). Therefore phosphorothioate modified oligonucleotides have the potential of

greater binding efficiency of the affinity molecule/charged carrier molecule conjugate to the analyte in the method of Kawabata et al. and Janssen et al.

11. Claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 51, 60-65, 67-75, 78-79, 84, 86, 88-89, 91-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US Patent 5571680 November 5, 1996) in view of Janssens et al. (US Patent 5611903 March 18, 1997).

With regard to Claim 1, Chen et al. teaches a method of detecting analyte of interest in a sample (abstract). With regard to step 1i, Chen et al. teaches a method contacting an analyte in a sample with an immunoglobulin containing a flurophore (column 5 lines 60-65). The immunoglobulin would be considered an affinity molecule.

Chen et al. teaches that the flurophore can be a BODIPY labeled oligonucleotide (Column 6 lines 43-45). Therefore Chen et al. teaches a charged carrier molecule complexed with an affinity molecule which has a charge because oligonucleotides have a negative charge.

Chen et al. teaches that the analyte in the sample can be a protein (column 7 lines 24-25) and that the immunoglobin can be a polyclonal antibody, a monoclonal antibody, an Fab fragment, an F(ab)2 fragments and a single chain immunoglobin (column 7 lines 30-35). Therefore the affinity molecule has an affinity against the analyte.

Chen et al. teaches that this complex can be separated from uncomplexed immunoglobulins (column 6 lines 1-5). Therefore this complex that includes the

charged carrier molecular has a change in the separation property of the analyte because it can be distinguishable from other complexes.

With regard to steps ii and iii. The instant specification does not define the term microfluidic device. Therefore the term is broadly interpreted as any microscopic component designed to handle liquid flow. Chen et al. teaches that a capillary electrophoresis device (e.g. a microfluidic device) is used to electrophoretically separate the complex of the analyte: affinity: carrier molecule from the unbound immunoglobin (e.g. the conjugate) (Column 6 lines 1-15). Chen et al. teaches that the capillary tube has an internal diameter (e.g. a separation channel) of from about 2 micrometers to about 2000 micrometers (Column 4 lines 20-25). Chen et al. teaches that a separation solution comprises buffers (e.g. separation media) (column 13 lines 13-20). However, Chen et al. does not teach a separation buffer with polyanions.

With regard to step iv, Chen et al. teaches a method of detecting the complex of the analyte:affinity:carrier molecule to identify the presences of the analyte (column 6 lines 6-8).

With regard to Claim 9, Chen et al. teaches a method with an immunoglobulin containing a flurophore (column 5 lines 60-65). The immunoglobulin would be considered an affinity molecule and it is labeled with a detectable marker.

With regard to claim 10, Chen et al. teaches that the sample can be incubated in the present of an immunoglobulin (e.g. without a flurophore) and an immunoglobulin with a flurophore (e.g. the conjugate) (Column 6 lines 50-57). Based upon the interpretation that the flurophore can comprise an oligonucleotide which would be

considered the charged carrier, Chen et al. teaches non-conjugated affinity molecules and conjugated molecules. Chen et al. teaches that the incubation is sufficient to form complexes with the sample analyte and the immunoglobulin (nonconjugate) and the sample analyte and the immunoglobulin with a flurophore (conjugate).

However, Chen et al. does not teach a complex of the analyte, an immunoglobin, and an immunoglobulin with a flurophore (e.g. a complex of the analyte, at least one conjugate and at least one non-conjugated affinity molecule). Chen et al. teaches a method wherein capillary electrophoresis can be use to separate complexes from free analytes and antigens based on size (column 24 lines 25-35). Therefore Chen et al. teaches that depending on the size of the complexes different complexes can be separated. Therefore it would be obvious to the ordinary artisan that any of the complexes made in a solution of analyte and affinity including a complex of an analyte with multiple affinity molecules can be separated. The ordinary artisan upon mixing conjugates, non-conjugates, and analytes would be able to determine that analyte can bind to a number of affinity molecules including both labeled and unlabeled immunoglobulins.

With regard to claims 11-12, Chen et al. teaches that the analyte in the sample can be a protein (column 7 lines 24-25) and that the immunoglobulin (affinity) can be a polyclonal antibody, a monoclonal antibody, an Fab fragment, an F(ab)2 fragments, a single chain immunoglobulin (column 7 lines 30-35). Therefore the binding can occur as a protein-protein interaction or an antigen-antibody interaction.

With regard to claim 13, Chen et al. teaches that the affinity molecule is selected from a polyclonal antibody, a monoclonal antibody, an Fab fragment, an F(ab)2 fragments and a single chain immunoglobulin (column 7 lines 30-35).

With regard to claims 14, 16, 17, and 18, Chen et al. teaches that the charged carrier molecule comprising DNA of a synthetic sequence (e.g. BODIPY labeled oligonucleotide) (Column 6 lines 43-45).

With regard to claims 19-21, Chen et al. provides an example of a fluorescent label comprises a synthetic oligonucleotides and an amino group linker (Column 25 lines 5-20).

With regard to Claims 22-23, Chen et al. teaches that analyte derivative contains a florescent moiety (column 7 lines 10-15). Therefore the analyte and the conjugate when complexed would be both labeled.

With regard to Claim 24-26, Chen et al. teaches that the charged carrier molecule comprising DNA of a synthetic sequence (e.g. BODIPY labeled oligonucleotide) (Column 6 lines 43-45). Therefore the complex of the charge carrier molecule, the affinity molecule and the analyte are labeled by the BODIPY label.

With regard to Claim 27, Chen et al. teaches a BODIPY dye (florescent dye) (column 6 lines 43-45).

With regard to claim 29, Chen et al. teaches that the separation media can comprise polyacrylamide gel (column 13 lines 15).

With regard to Claim 35, Chen et al. teaches that the capillary tube has an internal diameter (e.g. a separation channel) of from about 2 micrometers to about 2000 micrometers (Column 4 lines 20-25).

With regard to Claim 37, Chen et al. teaches a method of detecting analyte of interest in a sample (abstract). Chen et al. teaches a method of contacting an analyte in a sample with an immunoglobulin containing a flurophore (conjugate) (column 6 lines 50-56). Chen et al. teaches contacting the sample containing an analyte with an immunoglobin that does not comprises a flurophore (nonconjugate) (column 6 lines 50-56). The immunoglobulin would be considered an affinity molecule.

Chen et al. teaches that the flurophore can be a BODIPY labeled oligonucleotide (Column 6 lines 43-45). Therefore Chen et al. teaches a charged carrier molecule because oligonucleotides have a negative charge. Chen et al. teaches separating electrophoretically ((column 6 lines 58-63). Chen et al. teaches determining the amount of the analyte by detecting of the complexes (column 6 lines 63-66).

With regard to Claim 38, Chen et al. teaches that the sample can be incubated in the present of an immunoglobulin (nonconjugate) and a immunoglobulin with a flurophore (e.g. the affinity molecule/charged molecule conjugate) (Column 6 lines 50-57). Chen et al. teaches that the incubation is sufficient to form complexes with the sample and the immunoglobulin and the immunoglobulin with a flurophore.

However, Chen et al. does not teach a complex of the analyte, an immunoglobulin and an immunoglobulin with a flurophore. It would be obvious to the ordinary artisan that depending on the binding motifs of the analyte and the

immunoglobulin that multiple immunoglobulins can bind to the same analyte. Therefore complexes that involve both immunoglobulin, immunoglobulin with a flurophore, and an analyte can be produced (e.g. an analyte:nonconjugate: conjugate). Chen et al. teaches that the different analyte complexes can be separated and the affinity molecules which are complexed (Column 6 lines 58-63). Chen et al. teaches detecting the concentration of the analyte by separation of different complexes (column 6 lines 63-66).

With regard to Claim 39, Chen et al. teaches a method of detecting an analyte of interest in a sample (abstract). Chen et al. teaches that in one embodiment a labeled antigen is provided (e.g. a labeled analyte) to compete with unlabeled antigen of the sample (e.g. unlabeled analyte of the sample) for binding to a limiting amount of antibody (affinity) (column 11 lines 55-60). Chen et al. teaches that the antibody can be modified to complex with a negatively or positively charged moiety to facilitate the separation of the antibody for the antibody-antigen complex (column 14 lines 10-20).

Though with regard to the complex, Chen et al. teaches that the antibody is labeled and complexed with a negatively or positively charged moiety, it is obvious based on the further discussion of Chen with regard to labeling antigens (column 11 lines 55-60), that either the analyte or the affinity molecule can be labeled. Chen et al. teaches providing a CE column to resolve the separation (column 11 lines 35-38). However, Chen et al. does not teach that the separation media has the addition of a polyanion. Chen et al. teaches that the complexes are run on a high electrophoretic

mobility device to detect and determine the amount of the labeled analyte or the free labeled analyte based on separation mobility (abstract and column 11 lines 35-40).

With regard to Claims 41, 67, and 71, Chen et al. teaches a method of detecting an analyte of interest in a sample (abstract). Chen et al. teaches that in one embodiment a labeled antigen is provided (e.g. a labeled analyte) to compete with unlabeled antigen of the sample (e.g. unlabeled analyte of the sample) for binding to a limiting amount to the antibody (column 11 lines 55-60). Chen et al. teaches that the antibody can be modified to complex with a negatively or positively charged moiety to facilitate the separation of the antibody for the antibody-antigen complex (column 14 lines 10-20). Though with regard to the complex Chen et al. teaches that the antibody is labeled and complexed with a negatively or positively charged moiety, it is obvious based on the teaches of Chen with regard to labeling antigens (column 11 lines 55-60), that either the analyte or the affinity molecule can be labeled. Chen et al. teaches providing a CE column to resolve the separation (column 11 lines 35-38). However, Chen et al. does not teach that the separation media has the addition of a polyanion. Chen et al. teaches that the complexes are run on a high electrophoretic mobility device to detect and determine the amount of the labeled analyte or the free labeled analyte (abstract and column 11 lines 35-40).

With regard to Claim 43, Chen et al. teaches a method wherein the sample is blood, serum, cerebrospinal fluid, urine, milk, non-proteinaceous organic molecule, water, soli, waste, and foodstuff (column 7 lines 25-30).

With regard to Claim 51, this claim requires all the limitations of Claim 1 plus each charged carrier molecule has a net negative charge. As discussed with regard to Claim 1, the charged carrier molecule of Chen et al. has a net negative charge. Further the claims require a concentration channel filled with a concentration media and a polyanion. The instant specification does not define concentration media. Therefore the separation media would be considered a concentration media because a solution is poured into the capillary and only analytes are separated out thereby concentrating the analyte.

With regard to claims 60-62, Chen et al. teaches that the charged carrier molecule comprising DNA of a synthetic sequence (e.g. BODIPY labeled oligonucleotide) (Column 6 lines 43-45).

With regard to claims 63-65, Chen et al. provides an example of a fluorescent label comprises a synthetic oligonucleotides and an amino group linker (Column 25 lines 5-20).

With regard to claims 68-69, Chen et al. teaches that the analyte in the sample can be a protein (column 7 lines 24-25) and that the immunoglobulin (affinity) can be a polyclonal antibody, a monoclonal antibody, an Fab fragment, an F(ab)2 fragments, a single chain immunoglobulin (column 7 lines 30-35). Therefore the binding can occur as a protein-protein interaction or am antigen-antibody interaction.

With regard to claim 70 Chen et al. teaches that the affinity molecule is selected from a polyclonal antibody, a monoclonal antibody, an Fab fragment, an F(ab)2 fragments and a single chain immunoglobulin (column 7 lines 30-35).

With regard to Claim 72-74, Chen et al. teaches that the charged carrier molecule comprising DNA of a synthetic sequence (e.g. BODIPY labeled oligonucleotide) (Column 6 lines 43-45). Therefore the complex of the charge carrier molecule, the affinity molecule and the analyte are labeled by the BODIPY label.

With regard to Claim 75, Chen et al. teaches a fluorescent dye (BODIPY) (Column 6 lines 43-45).

With regard to Claim 86, Chen et al. teaches that the separation media can comprise polyacrylamide gel (column 13 lines 15).

With regard to Claim 92, Chen et al. teaches that the capillary tube has an internal diameter (e.g. a separation channel) of from about 2 micrometers to about 2000 micrometers (Column 4 lines 20-25).

However, with regard to steps ii-iv, Chen et al. does not teach that the separation channel is further filled with a polyanion.

With regard to Claims 1, 39, 41, and 51, Jansses et al. teaches adding a polyanion to a capillary buffer in a capillary electropherisis detection method (abstract). Jansses et al. teaches that the polyanion can be a polysaccharide derivative, a synthetic polymer derivative, a polyacidic amino acid, a polynucleotide, a polyphosphate, a polyphosphonate, a polyphosphoric acid, or heparin (column 9 lines 15-20 and table 2). Janssen et al teaches the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated (column 8 lines 1-6).

With regard to claims 3-4, Jansses et al. teaches that the polyanion can be a polysaccharide derivative, a synthetic polymer derivative, a polyacidic amino acid, a polynucleotide, a polyphosphate, a polyphosphonate, a polyphosphoric acid, or heparin (column 9 lines 15-20 and table 2).

With regard to claim 8, Jansses et al. teaches that the polyanion comprises heparin sulfate (table 2).

With regard to Claims 31 and 32, Jansses et al. teaches a method wherein the polyanion comprises about 1% by volume of the media in the capillary (column 10 lines 4-5).

With regard to Claim 44, Jansses et al. teaches hemoglobin variants (HBsAg) can be detected by capillary electrophoresis (Column 33 lines 24-26).

With regard to claims 78-79, Jansses et al. teaches that the polyanion can be a polysaccharide derivative, a synthetic polymer derivative, a polyacidic amino acid, a polynucleotide, a polyphosphate, a polyphosphonate, a polyphosphoric acid, or heparin (column 9 lines 15-20 and table 2).

With regard to claim 84, Jansses et al. teaches that the polyanion comprises heparin sulfate (table 2).

With regard to Claims 88-89, Jansses et al. teaches a method wherein the polyanion comprises about 1% by volume of the media in the capillary (column 10 lines 4-5).

With regard to claim 91, Jansses et al. teaches that polyanions comprise about 1% by volume and that one of the polyanions can be heparin sulfate (Column 10 lines 4-5 and Table 2).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify method of detecting or identifying an analyte of interest in a sample of Chen et al. to include in the step of providing a microfluidic device a separation channel which has a polyanion in a separation buffer as taught by Janssen et al. The ordinary artisan would have been motivated to modify the method of detecting or identifying an analyte of interest in a sample of Chen et al. to include in the step of providing a microfluidic device a separation channel which has a polyanion in a separation buffer as taught by Janssen et al., because Janssen et al teaches the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated (column 8 lines 1-6) therefore the use of polyanions allows for better elution of the analyte from complexes.

12. Claims 53, 55-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US Patent 5571680 November 5, 1996) in view of Janssens et al. (US Patent 5611903 March 18, 1997) as applied to Claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 51, 60-65, 67-75, 78-79, 84, 86, 88-89, 91-92 and further in view of Kaniansky et al. (Analytical chemistry 2000 Vol. 72 p. 3596).

Chen et al. and Janssens et al. teach a method of detecting or identifying an analyte of interest by electrophoretically separating an analyte couple to an

affinity/charged conjugate in a separation buffer comprising a polyanion. However, Chen et al. and Janssens et al. does not teach connecting the microchannel (e.g. the capillary column) to a concentration channel in the step of providing a microfluidic device having a separation channel.

With regard to Claims 53, Kaniansky et al. teaches a method of using a capillary electrophoresis chip with a two separation channel coupling (Abstract). Kaniansky et al. teaches using ITP (e.g. Concentration channel) as a concentration pretreatment of the analyte (Abstract). The claim requires at least one microscale dimension of between about 0.1 and 500 microns. The limitation does not require that the concentration channel be that size but rather the microfludiic device should have a microscale dimension of between about 0.1 and 500 microns. Chen et al. teaches that the capillary tube has an internal diameter (e.g. a separation channel) of from about 2 micrometers to about 2000 micrometers (Column 4 lines 20-25).

With regard to Claim 55, ITP is based on the mobility differences of the solution placed into the column, therefore, dependent on the size and charge of the components in the solution including the charged carrier, the components either get concentrated in a solution or trapped in the membrane. Therefore ITP utilized the charge of the complex (e.g. the charged carrier, the analyte, and the antigen) to move through the membrane whereas other components in the sample do not. Chen et al. further teaches the used of charges carriers causes sharper peaks in a capillary electrophoresis (column 14 lines 20-23) which indicate that based on the inclusion of the charged complex more of the analyte complex is separated out of the device.

With regard to claim 56, Chen et al. further teaches the use of charges carriers causes sharper peaks in a capillary electrophoresis (column 14 lines 20-23) which indicate that based on the inclusion of the charged complex more of the analyte complex is separated out of the device and less is absorbed onto the membrane of the device.

With regard to Claims 57-58, Kaniansky et al. teaches using isotachophoresis (ITP).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of detecting or identifying an analyte of interested in a sample of Chen et al. and Janssen et al. to include the ITP concentration method as taught by Kaniansky et al. in the step of providing a microfluidic device. The ordinary artisan would have been motivated to modify the method of detecting or identifying an analyte of interested in a sample of Chen et al. and Janssen et al. to include the ITP concentration method as taught by Kaniansky et al. in the step of providing a microfluidic device because Kaniansky et al. teaches using an ITP concentration pretreatment quantified test analytes by 1-2% RSD (Abstract). Kaniansky et al. teaches a well-defined ITP concentration of the analyte can be integrated into the separation method of a capillary channel chip (Abstract). By using the ITP concentration channel the ordinary artisan can increase the concentration of the analyte in the solution and thereby increase the detection and concentration of the analyte by the method of Chen et al.

13. Claim 66 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US Patent 5571680 November 5, 1996) in view of Janssens et al. (US Patent 5611903 March 18, 1997) as applied to Claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 51, 60-65, 67-75, 78-79, 84, 86, 88-89, 91-92 and further in view of Brown et al. (The journal of biological chemistry 1994 vol 269 p. 26801)

With regard to Claim 66, Chen et al. teaches that to analyze protein analytes a complex of a flurophore attached to one end of an oligonucleotide with an antigen attached to the other end of the oligonucleotide can be used (column 12 lines 45-50).

However, the combination of Chen et al. and Janssens et al. does not teach that the synthetic sequence (e.g. oligonucleotide) comprises phosphorothioate. Therefore Chen et al. and Janssens et al. does not teaches that in the step of analyzing protein analyte with a complex of a flurophore attached to the end of an oligonucleotide with an antigen attached to the other end of the oligonucleotide that the oligonucleotide is modified with phosphorothioate.

With regard to Claim 66, Brown et al. teaches a method of mobility shift assays which uses phosphorothiate-modified oligonucleotides (abstract). Brown et al. teaches that phosphorothioate modified oligonucleotides exhibit greater protein binding than unmodified oligonucleotides (abstract).

Therefore it would be prima facie obvious to modify the method of Chen et al. and Janssens et al. to further include a modification of the oligonucleotide of phosphorathiate of Brown et al. in the step of analyzing protein analytes with a complex of a flurophore attached to the end of an oligonucleotide with an antigen attached to the

other end of the oligonucleotide such that the oligonucleotide is modified with phosphorothioate. The ordinary artisan would be motivated to modify the oligonucleotide used in the method of Chen et al. and Janssens et al. to further include a modification of the oligonucleotide of phosphorathiate of Brown et al. in the step of analyzing protein analytes with a complex of a flurophore attached to the end of an oligonucleotide with an antigen attached to the other end of the oligonucleotide such that the oligonucleotide is modified with phosphorothioate because Brown et al. teaches phosphorothioate modified oligonucleotides exhibit greater protein binding than unmodified oligonucleotides (abstract). Therefore phosphorothioate modified oligonucleotides have the potential of greater binding efficiency in the method of Chen et al. and Janssens et al. because a greater protein binding potential would be observed between the protein analyte and the oligonucleotide in the conjugate.

14. Claim 93 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US Patent 5571680 November 5, 1996) in view of Janssen et al. (US Patent 5611903 March 18, 1997) and further in view of Kaniansky et al. (Analytical chemistry 2000 Vol. 72 p. 3596) as applied to claims 53, and 55-58 and further in view of Williams et al. (US Patent Application Publication 2002/0079223 June 27, 2002).

With regard to Claim 93, Chen et al. teaches a method of detecting analyte of interest in a sample (abstract). Chen et al. teaches a method contacting an analyte in a sample with an immunoglobulin containing a flurophore (column 5 lines 60-65). The immunoglobulin would be considered an affinity molecule. Chen et al. teaches that the

flurophore can be a BODIPY labeled oligonucleotide (Column 6 lines 43-45). Therefore Chen et al. teaches a charged carrier molecule complexed with an affinity molecule which has a charge because oligonucleotides have a negative charge.

Chen et al. teaches that the analyte in the sample can be a protein (column 7 lines 24-25) and that the immunoglobin can be a polyclonal antibody, a monoclonal antibody, an Fab fragment, an F(ab)2 fragments and a single chain immunoglobin (column 7 lines 30-35). Therefore the affinity molecule has an affinity against the analyte.

Chen et al. teaches that this complex can be separated from uncomplexed immunoglobulins (column 6 lines 1-5). Therefore this complex that includes the charged carrier molecular has a change in the separation property of the analyte because it can be distinguishable from other complexes.

Chen et al. teaches that a capillary electrophoresis device (e.g. a microfluidic device) is used to electrophoretically separate the complex of the analyte:affinity:carrier molecule from the unbound immunoglobin (e.g. the conjugate) (Column 6 lines 1-15). Chen et al. teaches that the capillary tube has an internal diameter (e.g. a separation channel) of from about 2 micrometers to about 2000 micrometers (Column 4 lines 20-25). Chen et al. teaches that a separation solution comprises buffers (e.g. separation media) (column 13 lines 13-20). However, Chen et al. does not teach a separation buffer with polyanions.

Chen et al. teaches a method of detecting the complex of the analyte:affinity:carrier molecule to identify the presences of the analyte (column 6 lines 6-8).

With regard to Claim 93, Janssen et al. teaches adding a polyanion to a capillary buffer in a capillary electrophoresis detection method (abstract). Janssen et al. teaches that the polyanion can be a polysaccharide derivative, a synthetic polymer derivative, a polyacidic amino acid, a polynucleotide, a polyphosphate, a polyphosphonate, a polyphosphoric acid, or heparin (column 9 lines 15-20 and table 2). Janssen et al teaches the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated (column 8 lines 1-6). Therefore Janssen et al. teaches electrophoretically separating the complex and any unbound conjugate in a separation media with a second polyanion.

With regard to Claim 93, Kaniansky et al. teaches a method of using a capillary electrophoresis chip with a two separation channel coupling (Abstract). Kaniansky et al. teaches using ITP (e.g. Concentration channel) as a concentration pretreatment of the analyte (Abstract). Kaniansky et al. teaches using a polyanion (methylhydroeythylcellulose) in the buffer solution for the ITP (Table 1).Therefore Kaniansky et al. teaches concentration the complex in a concentration channel filled with a first polyanion.

Therefore the combination of Chen et al., Janssen et al. and Kandinsky et al. teaches separating an analyte using a concentration channel with one polyanion and

then electrophrotically separating the complex and any unbound conjugate using a separation channel and a second polyanion.

However, the combination of Chen et al., Janssen et al. and Kaniansky et al. does not teach that the concentration channel in the step of providing a microfluidic device has at least one microscale dimension of between about 0.1 and 500 microns.

With regard to Claim 93, Williams et al. teaches that the ITP channel can be 250 microns (paragraph 62).

Therefore it would be prima facie obvious to the ordinary artisan to modify the method of Chen et al., Janssen et al, and Kandinsky et al. to use ITP channels that are of 250 microns in length as taught by Williams et al. in the step of providing a microfluidic device. It would have been obvious to one of ordinary skill in the art at the time the invention was made to choose from a finite number of micron lengths of ITP channels with a reasonable expectation of success of producing an ITP channel which can concentrate the analyte of the sample.

15. Claims 95-96, 98, and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US Patent 5571680 November 5, 1996) in view of Janssen et al. (US Patent 5611903 March 18, 1997) as applied to Claims 1, 3-4, 8-14, 16-27, 29, 31-32, 35, 37-39, 41, 43-44, 51, 60-65, 67-75, 78-79, 84, 86, 88-89, 91-92 and further in view of Kawabata et al. (WO 02/082083 A1 published 10/17/2002)

Citations are from the National Stage (US Patent Application 2004/0144649 July 29, 2004). The national stage is deemed an English language translation of the PCT.

Chen et al. and Janssen et al. teach a method detecting or identifying an analyte of interest in a sample comprising a step of electrophoretically separating an analyte couple to an affinity/charged conjugate in a separation buffer comprising a polyanion. Chen et al. does not teach a method which comprising contacting a sample containing an analyte with one affinity molecule/charged molecule conjugate, however, Chen et al. and Janssen et al. do not teach a method of using two or more conjugates wherein each affinity molecule in the two or more conjugates has a property capable of binding with the analyte at a different site on the analyte form every other affinity molecule.

With regard to Claims 95-96, 98, and 99, Kawabata et al. teaches a method for separation by electrophoresis which comprising forming 2 or more species of complexes (e.g. conjugates) (p. 3 paragraph 19). Kawabata et al. teaches that these two or more conjugates have an affinity only for specific targets in the analyte (p. 3 paragraph 20).

Therefore it would be prima facie obvious to one of ordinary skill in the art at the time of filing to modify the method of Chen et al. and Janssen et al. to in the step of contacting the sample, contact multiple analytes in the samples by using multiple conjugates of the affinity molecule/charged carrier molecule conjugates by using the teachings of Kawabata et al. which teaches that multiple analytes can be detected using multiple affinity molecules. The ordinary artisan would be motivated to modify the method of Chen et al. and Janssen et al. to use conjugates that have multiple affinities to different analytes because Kawabata et al. that it is possible to separate multiple species of complexes this way (p. 11 paragraph 119) and therefore the ordinary artisan

would be able to detect multiple target sites in one sample with one mobility run and therefore detect or identify analyte of interest in a sample.

16. Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hosokawa et al. (European Patent application EP1061370 A2 Date of publication 12/20/2000) in view of Janssen et al. (US Patent 5611903 March 18, 1997).

With regard to Claim 42, Hosokawa et al. teaches a method for determining an analyte in a sample (e.g. detection of CEAs) (abstract). Hosokawa et al. teaches a CEA binding antibody immobilized on an insoluble carrier is reacted with a sample derived from a living body (p. 7 lines 15-20). Therefore Hosokawa et al. teaches a method of binding an analyte to a charged carrier molecule because the CEA binding antibody would contain a charge. Hosokawa et al. teaches a labeled competitive CEA binding antibody (labeled affinity molecule), which is complexed to the analyte bound to the CEA binding antibody-insoluble carrier conjugate (p. 7 lines 25-35).

Thereby Hosokawa et al. teaches a first complex of an analyte bound to a charged carrier molecule and a labeled affinity molecule.

Hosokawa et al. teaches a method wherein competitive CEAs in the sample can be detected by further complexing nonbound CEAs (e.g. CEAs without the charged complex) to the labeled competitive CEAs binding antibody (p. 8 lines 20-25). Therefore Hosokawa et al. teaches the second complex.

Hosokawa et al. teaches that the affinity molecules are antibodies and therefore thy have affinity against the analyte.

Hosokawa et al. that the CEAs binding antibody coupled with the insoluble carrier (e.g. the charged carrier molecule) will affect the separation property because the analyte bound will be separated at a different time than the analyte which is not bound.

Hosokawa et al. teaches a method of separating the complexes and detecting the amounts of analytes (p. 13).

However, Hosokawa et al. does not teach providing a microfluidic device with a separation channel filled with a separation media and a polyanion.

With regard to Claim 42, Janssen et al. teaches adding a polyanion to a capillary buffer in a capillary electrophoresis detection method (abstract). Janssen et al. teaches that the polyanion can be a polysaccharide derivative, a synthetic polymer derivative, a polyacidic amino acid, a polynucleotide, a polyphosphate, a polyphosphonate, a polyphosphoric acid, or heparin (column 9 lines 15-20 and table 2). Janssen et al teaches the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated (column 8 lines 1-6).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Hosokawa et al. use in the step of providing a microfluidic device having a separation channel filled with a separation media and a polyanion in a separation buffer as taught by Janssen et al. The ordinary artisan would have been motivated to modify the method of Hosokawa et al. to use the polyanion in the separation buffer of the step of providing a microfluidic because Janssen et al teaches the use of a polyanion in a buffer allows for higher velocities and shorter migration times of complexes being separated (column 8 lines 1-6) therefore the use of polyanions allows for better elution of the analyte from complexes.

17. Claim 100 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hosokawa et al. (European Patent application EP1061370 A2 Date of publication 12/20/2000) in view of Janssen et al. (US Patent 5611903 March 18, 1997) as applied to Claim 42 and further in view of Kawabata et al. (WO 02/082083 A1 published 10/17/2002)

Citations are from the National Stage (US Patent Application 2004/0144649 July 29, 2004). The national stage is deemed an English language translation of the PCT.

Hosokawa et al. and Janssen et al. teach a method of electrophoretically separating two complexes of analyte based upon the sizes and mobility of analyte/labeled affinity and charged carrier/analyte/labeled affinity. However, Hosokawa et al. and Janssen et al. do not teach a method of using two or more affinity molecules are used and each affinity molecule has a property of binding at different sites.

With regard to 100, Kawabata et al. teaches a method for separation by electrophoresis which comprising forming 2 or more affinity molecules (p. 3 paragraph 19). Kawabata et al. teaches that these two or more affinity molecules bind to specific targets in the analyte (e.g. different sites) (p. 3 paragraph 20).

Therefore it would be prima facie obvious to one of ordinary skill in the art at the time of filing to modify the method of Hosokawa et al. and Janssen et al. to contact the sample more than one affinity molecules to detect the analyte in the sample as taught by Kawabata et al. The ordinary artisan would be motivated to modify the method of Hosokawa et al. and Janssen et al. to detect analytes by using multiple affinity

molecules as taught by Kawabata et al. because Kawabata et al. that it is possible to separate multiple species of analytes using multiple affinity molecules that are directed to different sites of the analyte (p. 11 paragraph 119) and therefore the ordinary artisan would be able to detect multiple target sites of the analyte with one mobility run.

Conclusion

18. No Claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Katherine Salmon/
Examiner, Art Unit 1634

/Ram R. Shukla/

Supervisory Patent Examiner, Art Unit 1634